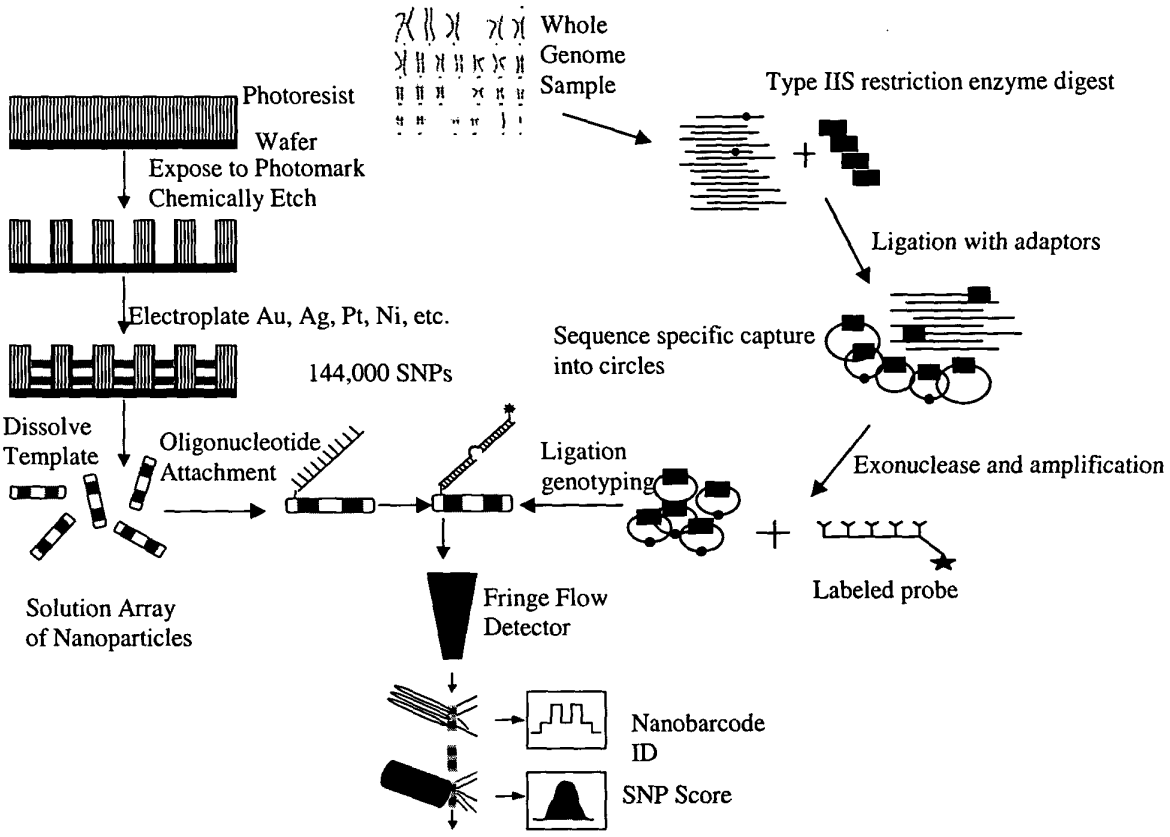

Whole Genome Sample
Type IIS restriction enzyme digest
Photoresist
Wafer
Expose to Photomark
Chemically Etch
Ligation with adaptors
Electroplate Au, Ag, Pt, Ni, etc.
144,000 SNPs
Sequence specific capture into circles
Dissolve Template
Oligonucleotide Attachment
Ligation genotyping
Exonuclease and amplification
Solution Array of Nanoparticles
Fringe Flow Detector
Labeled probe
Nanobarcode ID
SNP Score

Figure 1

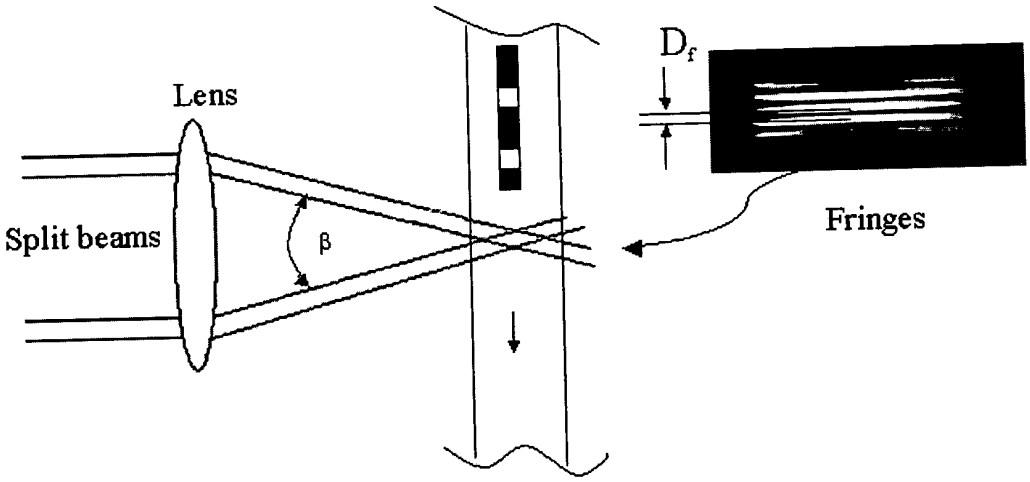


Figure 2

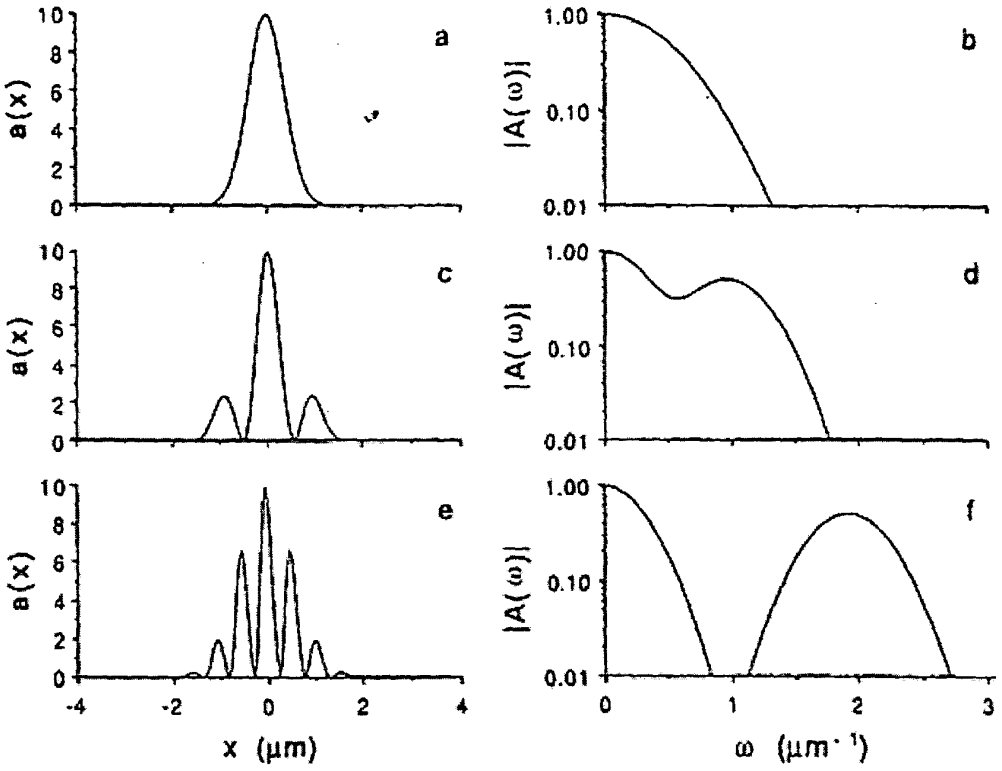


Figure 3

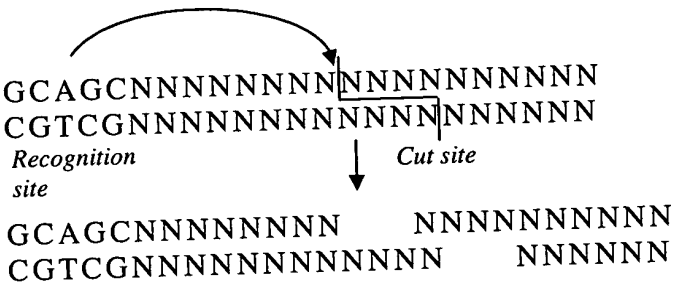

GCAGCNNNNNNNNNNNNNNNNNN
CGTCGNNNNNNNNNNNNNNNNNN
Recognition site
Cut site
GCAGCNNNNNNNN
NNNNNNNNNN
CGTCGNNNNNNNNNNNNN
NNNNNN

Figure 4

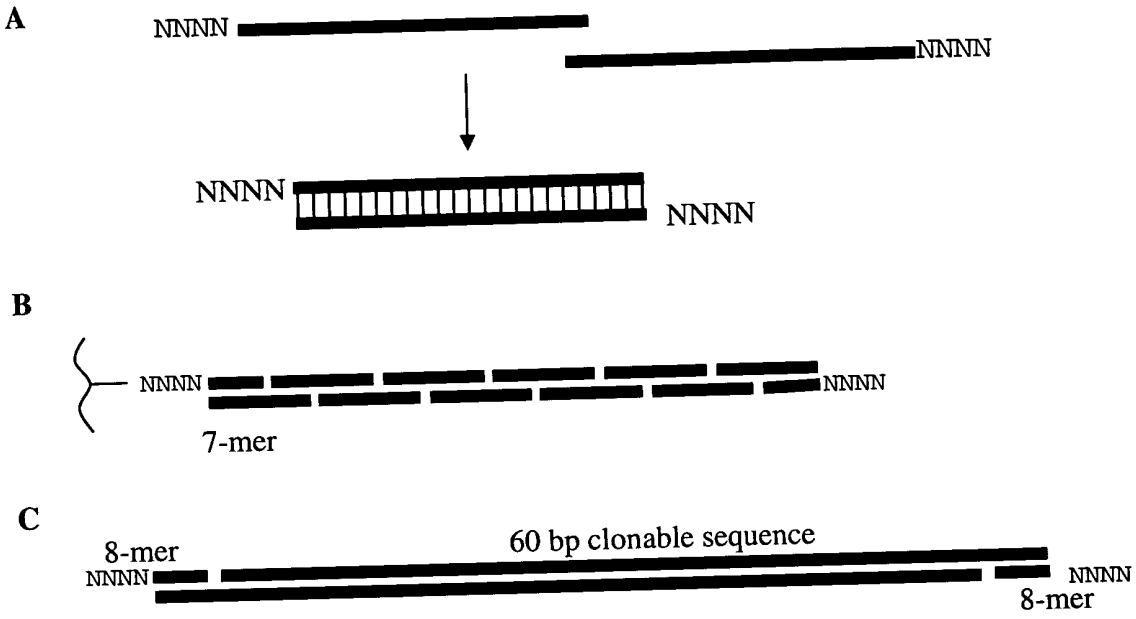

A
NNNN
NNNN
NNNN
NNNN
B
NNNN
NNNN
7-mer
C
8-mer
60 bp clonable sequence
NNNN
NNNN
8-mer

Figure 5

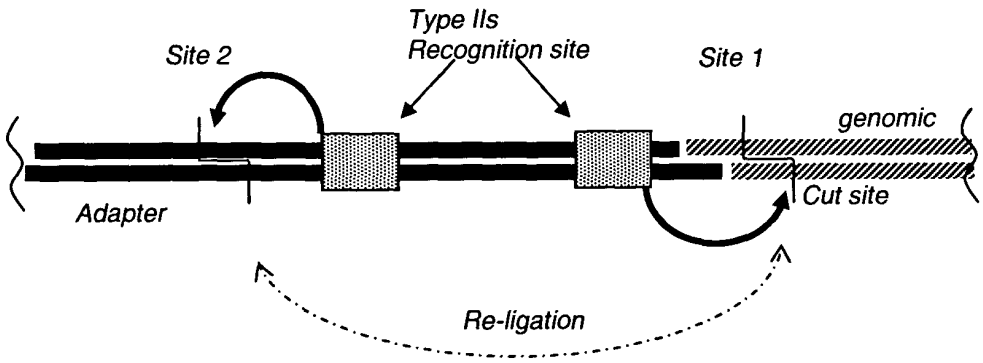

Type IIs
Recognition site
Site 2
Site 1
genomic
Adapter
Cut site
Re-ligation

Figure 6

A B B' C

Most frequent event: Adaptor binds one end, no circle formation

A B B' A'

Desired result: Adaptor and fragment ends match, ligate and circularize

A B B' A' A B

Ends match, but different adapters bind both ends, no circle formation; less frequent because intramolecular ligation after first adaptor attaches is very fast;

A B B' C C' A'

Two fragments ligate and circularize with an adaptor (chance to get one fragment with A' and one with B' overhang to ligate is 1 in 256, and most likely each will be blocked with an adaptor; multiple ligation is also slower)

A B B' A'

Two fragments ligate and circularize: low frequency because out-competed by adapters. No specific primer-binding site for amplification.

Figure 7

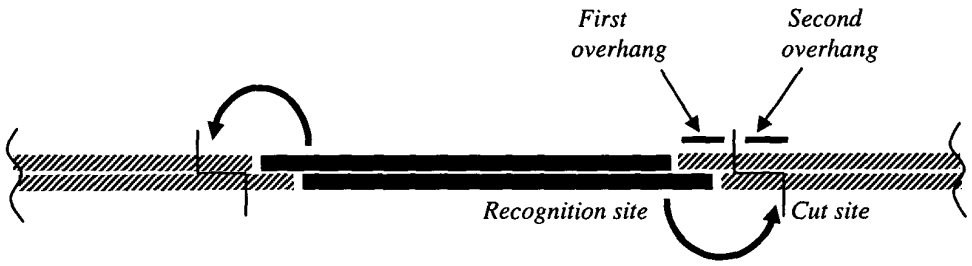


Figure 8

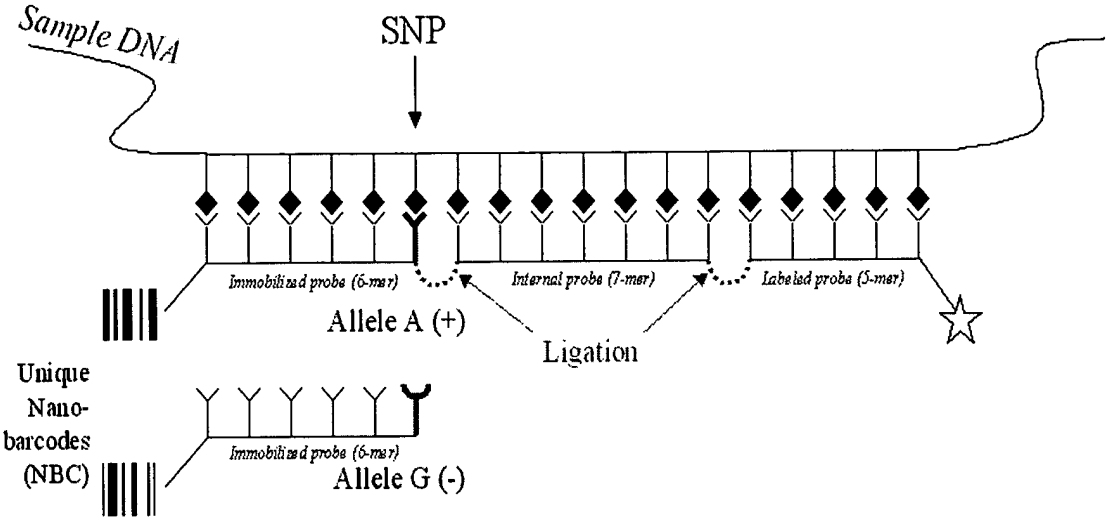

Sample DNA
SNP
Immobilized probe (6-mer)
Internal probe (7-mer)
Labeled probe (5-mer)
Allele A (+)
Ligation
Unique
Nano-
barcodes
(NBC)
Immobilized probe (6-mer)
Allele G (-)

Figure 9

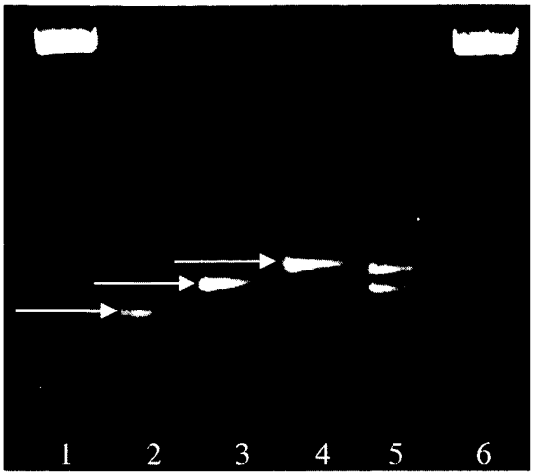


Figure 10A

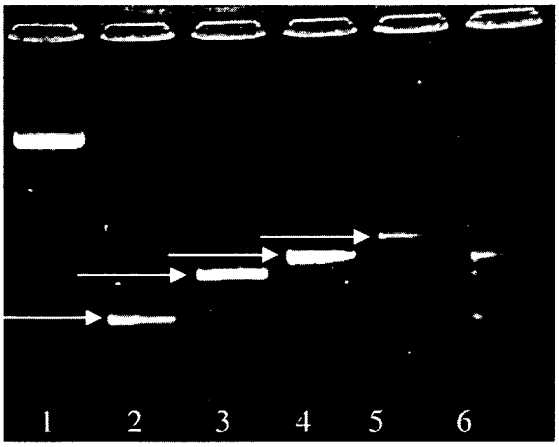
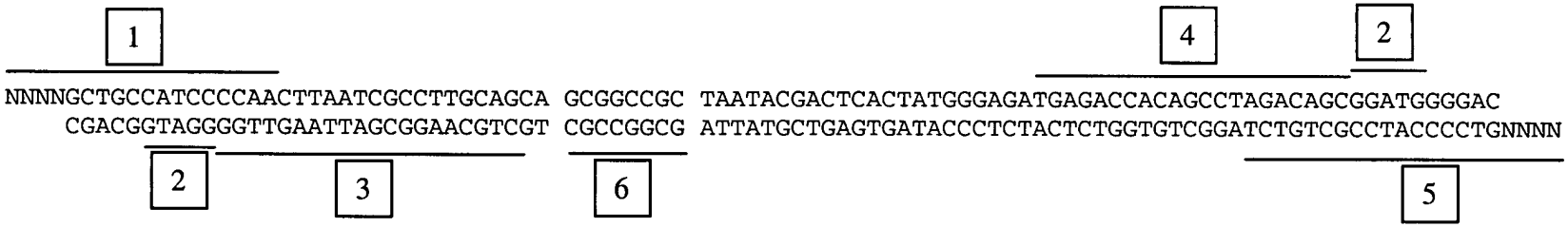


Figure 10B

Adapter A



1. Left overhang oligonucleotide
2. FokI recognition site
3. Left Primer binding site
4. Right primer binding site
5. Right overhang oligonucleotide
6. Not I site

Figure 11